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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant

Sherie L. Morrison et al.

Serial No.

08/266,154

Filed

June 27, 1994

For

METHODS FOR PRODUCING FUNCTIONAL IMMUNOGLOBULIN, INCLUDING CHIMERIC IMMUNOGLOBULIN, IN TRANSFORMED

MAMMALIAN LYMPHOCYTIC CELLS

Group Art Unit

1806

Examiner

Julie E. Reeves, Ph.D.

Hon. Assistant Commissioner for Patents

Washington, D.C. 20231

May 18, 1998

SECOND AMENDMENT AFTER ALLOWANCE PURSUANT TO 37 C.F.R. 1.312(a)

Sir:

Applicants request approval under Rule 312(a) for entry of the following amendment without withdrawing the case from issue.

of person

IN THE TITLE

Please replace the current title with:



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METHODS AND TRANSFORMED MAMMALIAN LYMPHOCYTIC CELLS FOR PRODUCING FUNCTIONAL ANTIGEN-BINDING PROTEIN INCLUDING CHIMERIC IMMUNOGLOBULIN AND FRAGMENTS

IN THE CLAIMS

Please amend claims 129-131 and 134-137 as follows:

34 129. A method as recited in claim 126 wherein [each] the first chain comprises a constant region.

A method as recited in claim 126 wherein the heavy and light chain variable domains are from [domain is found in] a first mammalian species and the heavy and light chain constant domains are from [domain is found in] a second mammalian species, said second mammalian species being other than the first mammalian species.

A method as recited in claim 125 wherein the heavy and light chain variable domains are from [domain is found in] a first mammalian species and the heavy and light chain constant regions are from [region is found in] a second mammalian species, said second mammalian species being other than the first mammalian species.

A method as recited in claim 132 wherein prior to step (a) the cell endogenously produces an immunoglobulin light chain or an immunoglobulin heavy chain, [which endogenously-produced heavy chain is not secreted in a form capable of specifically binding to antigen,] but not both.

[has] comprises a constant region.

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protein [immunoglobulin] comprises the heavy and light chain variable domains are from [domain found in] a first mammalian species and comprises the heavy and light chain constant domains are from [domain found in] a second mammalian species, said second mammalian species being other than the first mammalian species.

A method as recited in claim 135 wherein the antigen-binding protein [immunoglobulin] comprises the heavy and light chain variable domains are from [domain found in] a first mammalian species and comprises the heavy and light chain constant regions are from [region found in] a second mammalian species, said second mammalian species being other than the first mammalian species.

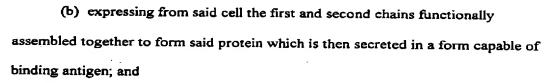
Please add the following claims 138-157.

A method for producing a functional antigen-binding protein comprising

- i) a first chain comprising an immunoglobulin heavy chain variable
 domain and an immunoglobulin heavy chain constant domain and
- ii) a second chain comprising an immunoglobulin light chain variable domain and an immunoglobulin light chain constant domain,

. wherein the method comprises the steps of:

(a) maintaining in a nutrient medium a transformed mammalian lymphocytic cell, said cell having been transfected with a first DNA molecule coding for the first chain of the protein and a second DNA molecule coding for the second chain of the protein;



(c) recovering said antigen-binding protein,

wherein prior to being transfected, the cell does not express a functional immunoglobulin capable of specifically binding antigen.

A method as recited in claim 138 wherein prior to step (a) the cell does not endogenously produce any immunoglobulin chains.

endogenously produces an immunoglobulin light chain or an immunoglobulin heavy chain, but not both.

A method as recited in claim 138 wherein the first chain comprises a constant region.

A method as recited in claim 138 wherein the heavy and light chain variable domains are from a first mammalian species and the heavy and light chain constant domains are from a second mammalian species, said second mammalian species being other than the first mammalian species.

A method as recited in claim 141 wherein the heavy and light chain variable domains are from a first mammalian species and the heavy and light chain constant regions are from a second mammalian species, said second mammalian species being other than the first mammalian species.

A transformed mammalian lymphocytic cell producing a functional antigen-binding protein comprising

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- i) a first chain comprising an immunoglobulin heavy chain variable
 domain and an immunoglobulin heavy chain constant domain and
- ii) a second chain comprising an immunoglobulin light chain variable domain and an immunoglobulin light chain constant domain,

wherein the transformed mammalian lymphocytic cell comprises:

- (a) a first exogenous DNA molecule coding for the first chain of the protein; and
- (b) a second exogenous DNA molecule, said second DNA molecule coding for the second chain of the protein; wherein without the exogenous DNA molecules the cell does not express a functional antigen-binding protein.
- wherein without the exogenous DNA molecules the cell does not endogenously produce any immunoglobulin chains.
- Wherein without the exogenous DNA molecules the cell endogenously produces an immunoglobulin light chain or an immunoglobulin heavy chain, but not both.
- 52-147. A transformed mammalian lymphocytic cell as recited in claim 144 wherein the first chain comprises a constant region.
- 53.148. A transformed mammalian lymphocytic cell as recited in claim. 144 wherein the heavy and light chain variable domains are from a first mammalian species and the heavy and light chain constant domains are from a second mammalian species, said second mammalian species being other than the first mammalian species.

Cont.

A transformed mammalian lymphocytic cell as recited in claim 147 wherein the heavy and light chain variable domains are from a first mammalian species and the heavy and light chain constant regions are from a second mammalian species, said second mammalian species being other than the first mammalian species.

55 ASO. A transformed mammalian lymphocytic cell producing a functional antigen-binding protein comprising

- i) a first chain comprising an immunoglobulin heavy chain variable
 domain and an immunoglobulin heavy chain constant domain and
- ii) a second chain comprising an immunoglobulin light chain variable
 domain and an immunoglobulin light chain constant domain,

wherein the transformed mammalian lymphocytic cell comprises:

a plasmid comprising a first exogenous DNA molecule coding for the first chain of the protein and a second exogenous DNA molecule coding for the second chain of the protein; and

wherein without the exogenous DNA molecules the cell does not express a functional antigen-binding protein.

wherein without the exogenous DNA molecules the cell does not endogenously produce any immunoglobulin chains.

wherein without the exogenous DNA molecules the cell endogenously produces an immunoglobulin light chain or an immunoglobulin heavy chain, but not both.

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58 153. A transformed mammalian lymphocytic cell as recited in claim 150 wherein the first chain comprises a constant region.

wherein the heavy and light chain variable domains are from a first mammalian species and the heavy and light chain constant domains are from a second mammalian species, said second mammalian species being other than the first mammalian species.

wherein the heavy and light chain variable domains are from a first mammalian species and the heavy and light chain constant regions are from a second mammalian species, said second mammalian species being other than the first mammalian species.

6) 456. A transformed mammalian lymphocytic cell produced by steps (a) and (b) of claim 126.

62 457. A transformed mammalian lymphocytic cell produced by step (a) of claim 132.

REMARKS

Applicants believe claims 138-157 are fully supported by the specification and respectfully request their entry and allowance.

Respectfully submitted,

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